

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (currently amended) A compound of the Formula Ia:



or a pharmaceutically acceptable salt thereof

wherein,

L- is a Ligand unit;

-A- is a Stretcher unit;

a is 1;

each -W- is independently an Amino Acid unit;

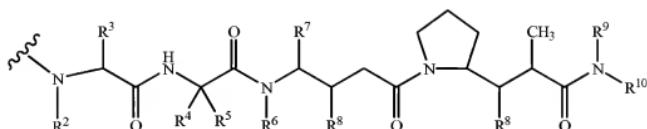
-Y- is a self-immolative Spacer unit;

w is an integer ranging from 2 to 12;

y is 1 or 2;

p ranges from 1 to about 20; and

-D is a Drug unit of the formula



wherein, the wavy line indicates the point of attachment to the Spacer unit,

and

independently at each location:

R² is selected from -H and -C₁-C₈ alkyl;

R³ is selected from -H, -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -O-(C₁-C₈ alkyl), -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle);

R^4 is selected from -H, -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -O-(C₁-C₈ alkyl), -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle) wherein R^5 is selected from -H and -methyl; or R^4 and R^5 join and form a ring with the carbon atom to which they are attached and R^4 and R^5 have the formula -(CR^aR^b)_n- wherein R^a and R^b are independently selected from -H, -C₁-C₈ alkyl and -C₃-C₈ carbocycle and n is selected from 2, 3, 4, 5 and 6;

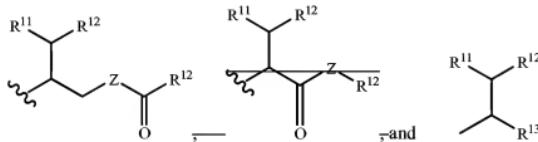
R^6 is selected from -H and -C₁-C₈ alkyl;

R^7 is selected from -H, -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -O-(C₁-C₈ alkyl), -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle);

each R^8 is independently selected from -H, -OH, -C₁-C₈ alkyl, -C₃-C₈ carbocycle and -O-(C₁-C₈ alkyl);

R^9 is selected from -H and -C₁-C₈ alkyl;

R^{10} is selected from



Z is -O-, -S-, -NH- or -N(R¹⁴)-;

R^{11} is selected from -H, -OH, -NH₂, -NHR¹⁴, -N(R¹⁴)₂, -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -O-(C₁-C₈ alkyl), -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle); or R^{11} is an oxygen atom which forms a carbonyl unit (C=O) with the carbon atom to which it is attached and a hydrogen atom on this carbon atom is replaced by one of the bonds in the (C=O) double bond;

each R^{12} is independently selected from -aryl and -C₃-C₈ heterocycle;

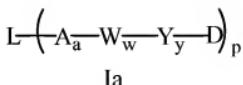
R^{13} is selected from -H, -OH, -NH₂, -NHR¹⁴, -N(R¹⁴)₂, -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -O-(C₁-C₈ alkyl), -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle); and

each R¹⁴ is independently -H or -C₁-C₈ alkyl.

2-6. (canceled)

7. (currently amended)

A compound of the formula Ia:



or a pharmaceutically acceptable salt thereof
wherein,

L- is a Ligand unit;

-A- is a Stretcher unit;

a is 1;

each -W- is independently an Amino Acid unit;

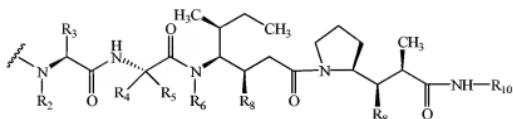
-Y- is a self-immolative Spacer unit;

w is an integer ranging from 2 to 12;

y is 1 or 2;

p ranges from 1 to about 20; and

-D is a Drug unit having the structure



or a pharmaceutically acceptable salt thereof,
wherein, the wavy line is the point of attachment to the Spacer unit, and
independently at each location:

R² is selected from -H and -methyl;

R³ is selected from -H, -methyl, and -isopropyl;

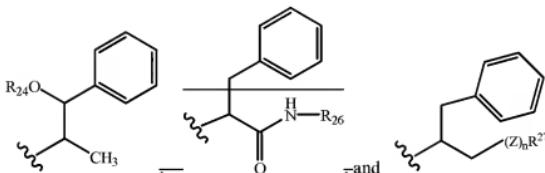
R⁴ is selected from -H and -methyl;

R⁵ is selected from -isopropyl, -isobutyl, -sec-butyl, -methyl and -t-butyl or R⁴ and R⁵ join and form a ring with the carbon atom to which they are attached and R⁴ and R⁵ have the formula -(CR³R^b)_n where R^a and R^b are independently selected from -H, -C₁-C₈ alkyl, and -C₃-C₈ carbocycle, and n is selected from 2, 3, 4, 5 and 6;

R⁶ is selected from -H and -methyl;

each R⁸ is independently selected from -OH, -methoxy and -ethoxy;

R¹⁰ is selected from



R²⁴ is selected from H and -C(O)R²⁵; wherein R²⁵ is selected from -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle);

Z is -O-, -NH-, -OC(O)-, -NHC(O)-, -NR²⁸C(O)-; where R²⁸ is selected from -H and -C₁-C₈ alkyl;

n is 0 or 1; and

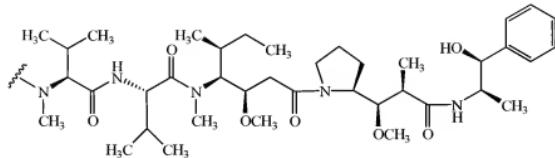
R²⁶ is selected from -C₄-C₈ alkyl, -C₃-C₈ carbocycle, aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl (C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl (C₃-C₈ heterocycle);

R²⁷ is selected from -H, -N₃, -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle) when n is 0; and

R²⁷ is selected from -H, -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle) when n is 1.

8. (canceled)

9. (previously presented) A compound or a pharmaceutically acceptable salt of the compound of claim 1 where -D is a Drug unit having the structure



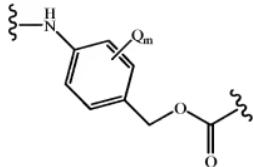
10-16. (canceled)

17. (previously presented) A compound or a pharmaceutically acceptable salt of the compound of claim 1 where the Ligand unit is an antibody.

18. (previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 17 where the antibody unit is a monoclonal antibody.

19. (previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 18 where the monoclonal antibody specifically binds the CD30 antigen, the CD70 antigen, the CD20 antigen, or the Lewis antigen.

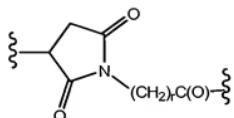
20. (previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -Yy- is



Q is selected from -C₁-C₈ alkyl, -O-(C₁-C₈ alkyl), -halogen, -nitro and -cyano; and

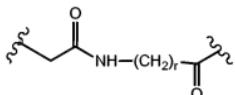
m is an integer ranging from 0-4, the amino terminus of -Yy- forming a bond with the Amino acid unit and the carboxyl terminus of -Yy- forming a bond with the Drug unit.

21. (previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



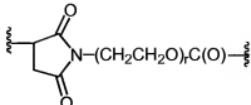
and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino Acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

22. (withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



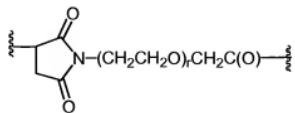
and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino Acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

23. (withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



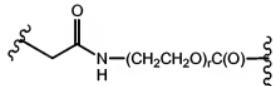
and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

24. (withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



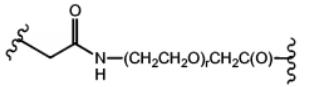
and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

25. (withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



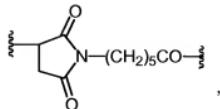
and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

26. (withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



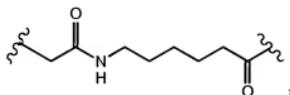
the carbonyl terminus of -A- forming a bond with the Amino acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

27. (previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 21 where -A- is



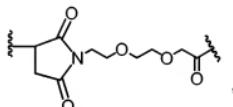
the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

28. (withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 22 where -A- is



the carbonyl terminus of -A- forming a bond with the Amino acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

29. (withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 24 where -A- is

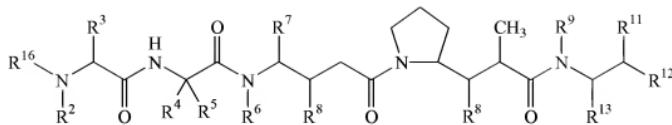


the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

30. (withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -W_w- is -Phenylalanine-Lysine-, the amino terminus of -W_w- forming a bond with the Stretcher unit and the C- terminus of -W_w- forming a bond with the Spacer unit.

31-43. (canceled)

44. (withdrawn) A compound of the formula



or a pharmaceutically acceptable salt thereof

wherein, independently at each location:

R² is selected from -H and -C₁-C₈ alkyl;

R³ is selected from -H, -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -O-(C₁-C₈ alkoxy), -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle);

R⁴ is selected from -H, -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -O-(C₁-C₈ alkoxy), -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle) wherein R⁵ is selected from -H and -methyl; or R⁴ and R⁵ join and form a ring with the carbon atom to which they are attached and R⁴ and R⁵ have the formula -(CR^aR^b)_n wherein R^a and R^b are independently selected from -H, -C₁-C₈ alkyl and -C₃-C₈ carbocycle and n is selected from 2, 3, 4, 5 and 6;

R⁶ is selected from -H and -C₁-C₈ alkyl;

R⁷ is selected from -H, -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -O-(C₁-C₈ alkoxy), -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle);

each R⁸ is independently selected from -H, -OH, -C₁-C₈ alkyl, -C₃-C₈ carbocycle and -O-(C₁-C₈ alkoxy);

R⁹ is selected from -H and -C₁-C₈ alkyl;

R¹¹ is selected from -H, -OH, -NH₂, -NHR¹⁴, -N(R¹⁴)₂, -C₁-C₈ alkyl, -C₃-C₈ carbocycle, -O-(C₁-C₈ alkyl), -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle); or R¹¹ is an oxygen atom which forms a carbonyl unit (C=O) with the carbon atom to which it is attached and a hydrogen atom on this carbon atom is replaced by one of the bonds in the (C=O) double bond;

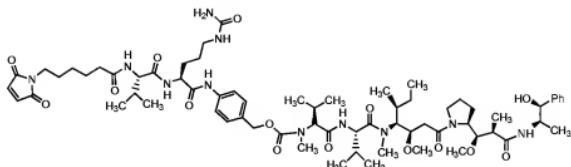
each R^{12} is independently selected from -aryl and -C₃-C₈ heterocycle;
 R^{13} is selected from -H, -OH, -NH₂, -NHR¹⁴, -N(R¹⁴)₂, -C₁-C₈ alkyl,
-C₃-C₈ carbocycle, -O-(C₁-C₈ alkoxy), -aryl, -C₁-C₈ alkyl-aryl, -C₁-C₈ alkyl-(C₃-C₈ carbocycle), -C₃-C₈ heterocycle and -C₁-C₈ alkyl-(C₃-C₈ heterocycle);
each R^{14} is independently -H or -C₁-C₈ alkyl;
 R^{16} is A'a-Ww-Yy-

wherein

each -W- is independently an Amino Acid unit;
-Y- is a self-immolative Spacer unit;
w is an integer ranging from 2 to 12;
y is 1 or 2;
-A' is a Stretcher unit; and
a is 1.

45. (withdrawn)

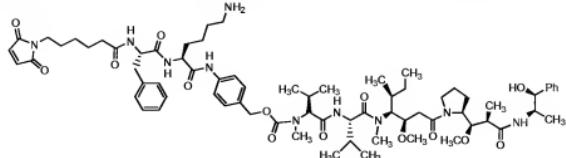
The compound of claim 44 having the structure



or a pharmaceutically acceptable salt thereof.

46. (withdrawn)

The compound of claim 44 having the structure

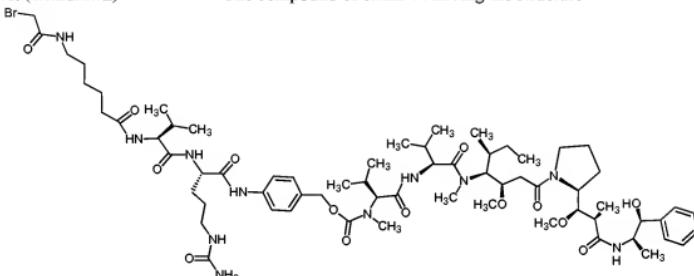


or a pharmaceutically acceptable salt thereof.

47. (canceled)

48. (withdrawn)

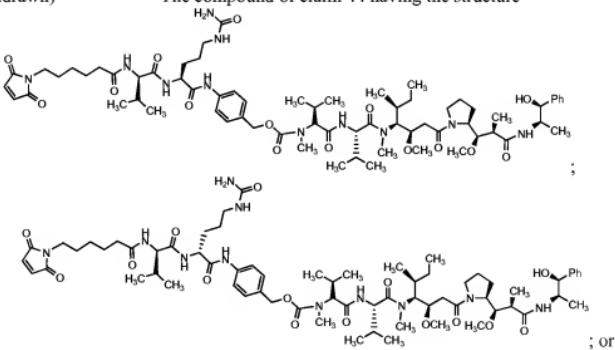
The compound of claim 44 having the structure

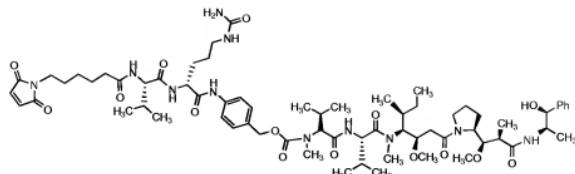


or a pharmaceutically acceptable salt thereof.

49. (withdrawn)

The compound of claim 44 having the structure

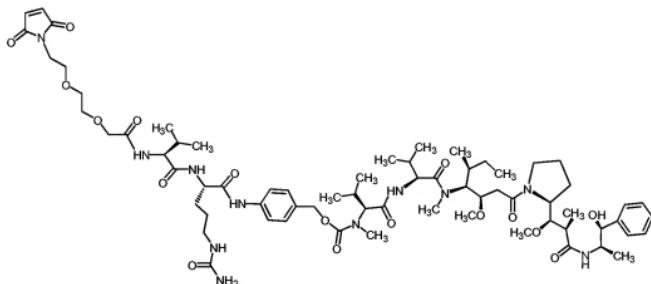




or a pharmaceutically acceptable salt thereof.

50-51. (canceled)

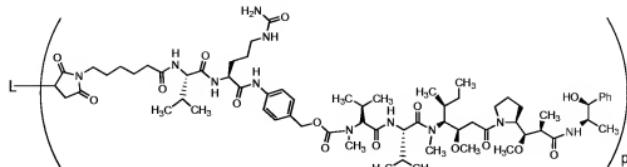
52. (withdrawn) The compound of claim 44 having the structure



or a pharmaceutically acceptable salt thereof.

53. (canceled)

54. (previously presented) The compound of claim 1 having the structure

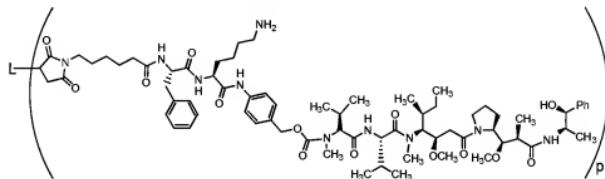


where p ranges from 1 to about 20, or a pharmaceutically acceptable salt thereof.

55. (canceled)

56. (withdrawn)

The compound of claim 1 having the structure

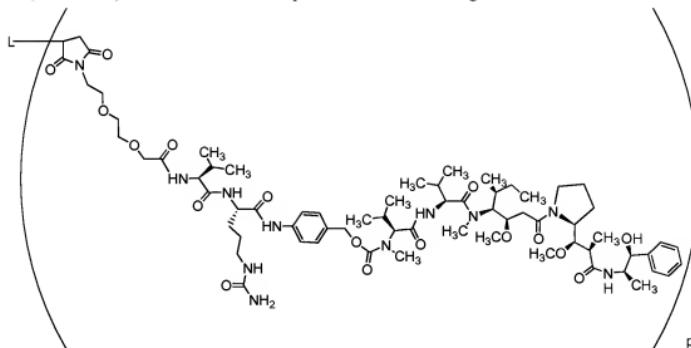


where p ranges from 1 to about 20, or a pharmaceutically acceptable salt thereof.

57-58. (canceled)

59. (withdrawn)

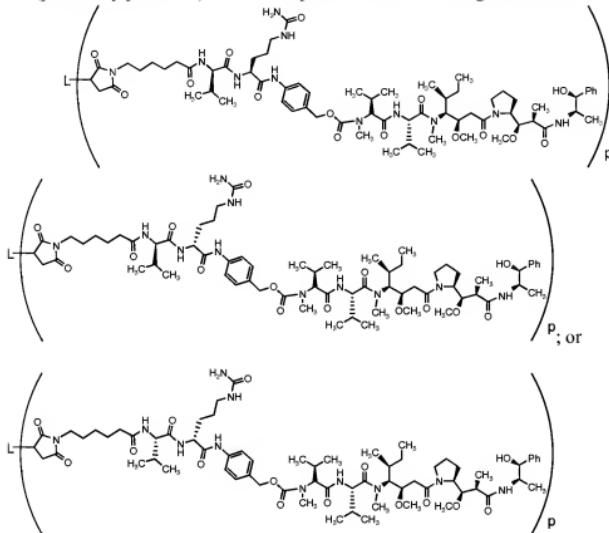
The compound of claim 1 having the structure



where p ranges from 1 to about 20, or a pharmaceutically acceptable salt thereof.

60-62. (canceled)

63. (previously presented) The compound of claim 1 having the structure



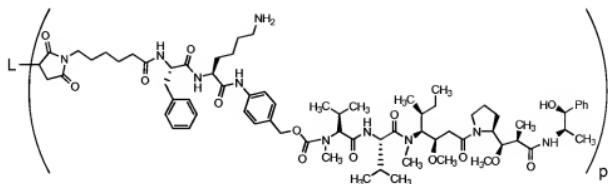
where p ranges from 1 to about 20, or a pharmaceutically acceptable salt thereof.

64-65. (canceled)

66. (previously presented) The compound of claim 54 where p ranges from about 1 to about 8.

67-76. (canceled)

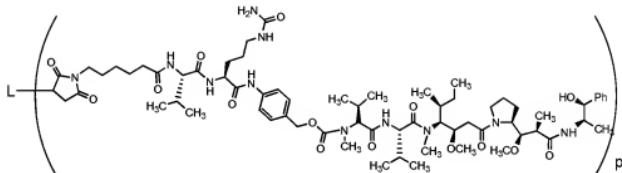
77. (withdrawn) The compound of claim 1 having the formula



or a pharmaceutically acceptable salt thereof, where p ranges from about 1 to about 8 and L is a monoclonal antibody.

78. (canceled)

79. (previously presented) The compound of claim 1 having the formula



or a pharmaceutically acceptable salt thereof, where p ranges from about 1 to about 8 and L is a monoclonal antibody.

80-99. (canceled)

100. (withdrawn) The compound or pharmaceutically acceptable salt thereof of claim 79 wherein L specifically binds the CD20 antigen.

101-103. (canceled)

104. (withdrawn) The compound or pharmaceutically acceptable salt thereof of claim 77 wherein L specifically binds the CD20 antigen.

105-110. (canceled)

111. (previously presented) A composition comprising an effective amount of a compound or a pharmaceutically acceptable salt thereof of claim 1 and a pharmaceutically acceptable carrier or vehicle.

112-118. (canceled)

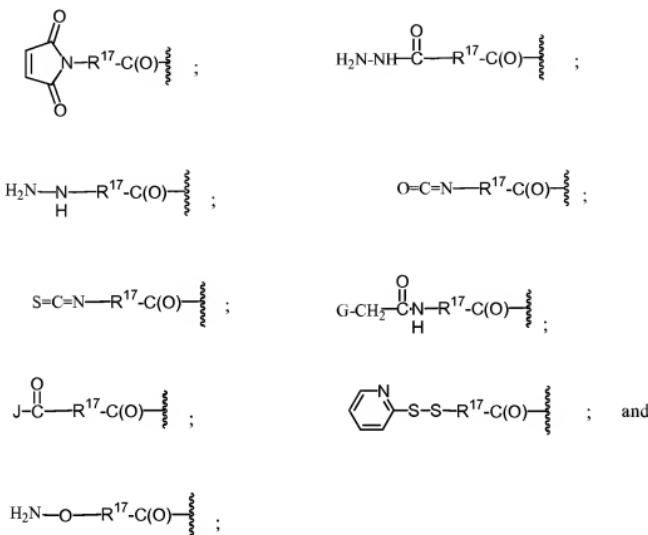
119. (previously presented) The compound or a pharmaceutically acceptable salt thereof of claim 1 in an isolated or a purified form.

120. (canceled)

121. (previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -W_w- is-valine-citrulline-, the amino terminus of -W_w- forming a bond with the Stretcher unit, and the C- terminus of -W_w- forming a bond with the Spacer unit.

122. (withdrawn) The compound of claim 44 or a pharmaceutically acceptable salt of the compound of claim 44, wherein

-A' is selected from



wherein

G is selected from -Cl, -Br, -I, -O-mesyl and -O-tosyl];

J is selected from -Cl, -Br, -I, -F, -OH, -O-N-succinimide, -O-(4-nitrophenyl), -O-pentafluorophenyl, -O-tetrafluorophenyl and -O-C(O)-OR¹⁸.

a is 1:

R^{17} is selected from $-C_1-C_{10}$ alkylene-, $-C_3-C_8$ carbocyclo-, $-O-(C_1-C_8$ alkoxy)-, $-arylene-$, $-C_1-C_{10}$ alkylene-arylene-, $-arylene-C_1-C_{10}$ alkylene-, $-C_1-C_{10}$ alkylene-(C_3-C_8 carbocyclo)-, $-(C_3-C_8$ carbocyclo)- C_1-C_{10} alkylene-, $-C_3-C_8$ heterocyclo-, $-C_1-C_{10}$ alkylene-(C_3-C_8 heterocyclo)-, $-(C_3-C_8$ heterocyclo)- C_1-C_{10} alkylene-, $-(CH_2CH_2O)_r$, and $-(CH_2CH_2O)_r-CH_2-$:

r is an integer ranging from 1-10; and

R^{18} is $-C_1-C_8$ alkyl or $-ar$ yl.

123. (canceled).

124. (previously presented) A composition comprising an effective amount of a compound or a pharmaceutically acceptable salt thereof of claim 79 and a pharmaceutically acceptable carrier or vehicle.

125. (previously presented) A composition comprising an effective amount of a compound or a pharmaceutically acceptable salt thereof of claim 121 and a pharmaceutically acceptable carrier or vehicle.

126. (previously presented) The compound or a pharmaceutically acceptable salt thereof of claim 79 in an isolated or a purified form.

127. (previously presented) The compound or a pharmaceutically acceptable salt thereof of claim 121 in an isolated or a purified form.

128. (withdrawn) The compound of claim 56 where p ranges from about 1 to about 8.

129. (withdrawn) The compound of claim 59 where p ranges from about 1 to about 8.

130. (previously presented) The compound of claim 63 where p ranges from about 1 to about 8.

131. (new) The compound or pharmaceutically acceptable salt thereof of claim 1 where R¹⁰ is



132. (new) The compound or pharmaceutically acceptable salt thereof of claim 7 where R¹⁰ is

